REMARKS

Claims 1-4, 15, 16, 20, 47, 48, 51, 56, 57, 60, 86-90, and 98 were previously pending in this application. By this amendment, Applicants are canceling claims 3, 6, 20, 51, 56, 57, 60, and 90 without prejudice or disclaimer. Claims 6, 20, 51, 56, 57, 60, and 90 were previously withdrawn. Claims 1, 15, 47, 86, and 98 have been amended. Claims 1, 2, 4, 15, 16, 20, 47, 48, 51, 56, 57, 60, 86-89, and 98 are pending for examination with claims 1, 15, 47, 86, and 98 being independent claims. In addition to the claim amendments described below, claim 15 has also been amended to replace the word "form" with the word "from" to correct the typographical error. No new matter has been added.

Applicants would like to thank the Examiners for the courtesy extended in granting the telephonic interview.

Objections

Applicants have amended claims 1, 15, 47, 86, and 98, and have cancelled claim 3 to remove subject matter that was non-elected due to the restriction requirement election.

Rejections Under 35 U.S.C. §112, second paragraph

The Examiner rejected claims 15, 16, and 98 under 35 U.S.C. §112, second paragraph as indefinite. The Examiner indicates that it is unclear as to whether the second sample is obtained from the same subject as the first sample. Applicants have amended claims 15 and 98 to replace the word "a" with the word "the" to indicate that the second sample is obtained from the same subject as the first sample.

Applicants respectfully request the Examiner withdraw the rejection of claims 15, 16, and 98 under 35 U.S.C. §112, second paragraph.

Rejections Under 35 U.S.C. §101

The Examiner has maintained the rejection of claims 1-4, 15, 16, 47, 48, 86-89, and 98 as lacking utility. Applicants respectfully traverse the rejection.

Examiners Dune Ly and Ardin Marschel conducted a telephone interview on January 28, 2004 with Applicants' representatives John Van Amsterdam and MaryDilys Anderson, and

Assignee's representative Dr. Pär Olsson to address the issues underlying the rejection of claims 1-4, 15, 16, 47, 48, 86-89, and 98 under 35 U.S.C. §101. At the conclusion of the interview, Examiners Ly and Marschel requested that Applicants summarize the content of the interview in the response to the Office Action mailed November 14, 2003. Applicants provide the following summary of the telephone interview.

The interview began with a summary of the claimed invention and related field of cancer diagnostics by Dr. Pär Olsson. The summary included a description of the art-recognized immune response in cancer, which is useful as an indication of cancer in a subject. Examiner Marschel requested Applicants to provide review articles that describe the immune response in cancer. Copies of Sahin et al., *Curr. Opin. Imm.* 1997, 9:709-716 and O.J. Finn, *Nature*, 2003, 3:630-641 are submitted herewith to comply with Examiner Marschel's request. These articles provide a review of the SEREX method and the identification of tumor antigens recognized by the immune system using that method. Applicants submit that similar information is also provided in the Scalan et al., *Int. J. Cancer* 1998, 76:652-658, a replacement copy of which was submitted to the Examiner with July 18, 2003.

The methods set forth in these publications were summarized by Dr. Olsson in the telephone interview. Dr. Olsson described the process by which the proteins that give rise to the immune response in cancer were identified by Applicants using SEREX methodology. Dr. Olsson indicated that the polypeptides that Applicants have identified as giving rise to an immune response in cancer can be used to diagnose cancer and to monitor the efficacy of treatment of cancer in patients. Dr. Olsson explained that the claimed methods of diagnosing cancer include contacting sera obtained from a subject with a panel of polypeptides identified by Applicants as expressed in patients with cancer but not expressed "normal" patients. After contacting the polypeptide panel with the sera, one can determine whether antibodies are present in the subject's sera that recognize a polypeptide of the panel, i.e., whether the subject has mounted an immune response against the polypeptide. The presence of such antibodies in the sera is an indication of cancer in that subject. Dr. Olsson also described that the diagnostic methods of the invention can be used to assess the efficacy of cancer treatments through the determination of changes in the presence or level of antibodies to the polypeptides of the invention over the course of cancer treatment.

Examiner Ly requested additional information regarding the manner with which genes encoding the polypeptides of the invention were identified. Dr. Olsson described the process through which a sequence library was screened for clones, clones were harvested, and the sequences obtained was compared with Genbank sequences to identify the genes. Dr. Olsson explained that although the method of obtaining the sequences via the screening and identification process is step utilized by Applicants to identify the antigenic polypeptides, the claimed invention is the use of the polypeptide sequences identified by Applicants, in the claimed cancer diagnostic methods.

Examiner Marschel then suggested that there are many different ways to make libraries and that the libraries may only include pieces but not full-length sequences. Applicants' representative agreed that this can be true of libraries, but because the polypeptides utilized in the assays of the invention were identified by Applicants because they give rise to antibodies in sera, the polypeptides must be expressed in patients as functional proteins. Examiner Marschel then inquired about the form of the vectors used in the process to isolate and identify the sequences of the invention, specifically asking whether the sequences themselves included transcription and translation control sequences, or whether such were provided as part of the vector. Applicants' representative explained that although some expression vectors do provide control sequences, it is the fact that the polypeptide is recognized by antibodies in sera that is important, irrespective of the location of the control sequences. Dr. Olsson concurred and stated that the Applicants had expressed the polypeptides in *E. coli* using a vector-provided promoter, and that the product of the expression was a protein that is recognized by antibodies that react with native protein, e.g. a protein that has induced an immune response in a patient with cancer.

Examiner Marschel then asked whether the specification included supporting data concerning the detection of the immune response and antibodies in sera of colon cancer patients versus sera obtained from "normal" individuals. Dr. Olsson indicated that the data requested by the Examiner is present at in the specification at page 33, in Table 1. Examiner Marschel also referred to aspects of the Sahin et al, *Proc. Natl. Acad. Sci. USA* 1995, 92:11810-11813 paper, specifically at page 11812, left hand column, which he proposed might suggest that some antigens that arise in disease may be present in patients who are "normal", not just patients with the disease of interest. Dr. Olsson indicated that the Sahin et al. reference was the first

publication on the SEREX method and that the understanding of SEREX has advanced since its publication nine years ago. Dr. Olsson agreed that some antigens have been found to be expressed in "normal" as well as patients with a disease of interested, but reiterated that of *none* of the fifteen polypeptides claimed for use in the instant diagnostic methods are present in normal serum, as shown by the data in the application as filed.

At the conclusion of the telephone interview Examiner Ly requested that Applicants provide a summary of the content of the interview and indicated that the Examiners would reconsider the rejections in light of the discussion.

As clarified in the telephone interview, Applicants respectfully assert that they have provided one or more utilities that are substantial, credible, and specific to the claimed invention. For example, the nucleic acid molecules and polypeptides encoded by the nucleic acid molecules can be used in claimed methods for the diagnosis of cancer and/or assessment of treatment of cancer in a subject. Based on the knowledge of one of ordinary skill in the art, the disclosed utilities in cancer diagnostic methods are also well established

Based on specification as filed and on the arguments presented in the telephonic interview of January 28, 2004, which is summarized above, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1, 2, 4, 15, 16, 47, 48, 86-89, and 98 under 35 U.S.C. § 101.

Rejections Under 35 U.S.C. §112, first paragraph

Enablement

The Examiner rejected claims 1-5, 15, 16, 47, 48, 86-89, and 98 under 35 U.S.C. §112, first paragraph for lack of enablement. Applicants respectfully traverse the rejection and assert that the claimed invention is enabled throughout its scope.

Applicants reiterate the arguments presented in the response filed July 15, 2003, and request reconsideration by the Examiner in light of the telephonic interview of January 28, 2004, which is summarized above. In view of the demonstrated utility of the claimed methods, Applicants assert that the pending claims are fully enabled.

As is there is no other basis for the enablement rejection, Applicants respectfully request the Examiner to withdraw the rejection of claims 1, 2, 4, 15, 16, 47, 48, 86-89, and 98 under 35 U.S.C. §112 first paragraph.

CONCLUSION

In view of the foregoing amendments and remarks, this application should now be in condition for allowance. A notice to this effect is respectfully requested. If the Examiner believes, after this amendment, that the application is not in condition for allowance, the Examiner is requested to call the Applicants' representative at the telephone number listed below.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicants hereby request any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

Respectfully submitted,
Yao-Tseng Chen et al., Applicant

By: _____

MaryDilys S. Anderson, Reg. No.52,560
Wolf, Greenfield & Sacks, P.C.
600 Atlantic Avenue
Boston, Massachusetts 02210-2211
Telephone: (617) 720-3500

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